REMARKS

Claims 1-21 are pending in this application. By this amendment, claims 11-13 are cancelled, claims 1-7, 9, 10, and 14 are amended, and new claims 22-36 are added. Following entry of this amendment, claims 1-10 and 14-36 will be pending. No new matter is added. Entry of this amendment is respectfully requested.

Support for the amendments and new claims is found throughout the specification, including, for example, at page 8, lines 14-15; page 27, line 26 to page 28, line 2; page 66, lines 29-30; page 3, lines 22, 25, and 29; page 4, line 2; page 8, lines 17-20; page 15, lines 1-2, 7-8, and 16-23; and page 71, line 1. In addition to amendments described below, claims 1, 5, 6, 7, 9, and 10 are amended to recite "polynucleotide" (rather than "DNA"). Claims 2, 4, 9 and 10 are amended to recite "polynucleotide (rather than "nucleotide", "nucleic acid", or "nucleic acid sequence") to clarify the claims and increase consistency of claim language. Claims 9 and 10 are amended to add "from about" to clarify the claims and improve consistency of claim language.

With respect to all new and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any objection and/or rejection made by the Office. Applicants expressly reserve the right to pursue prosecution of any subject matter not presently claimed in one or more future or pending continuation and/or divisional applications.

Pursuant to MPEP § 2001.06(b), the Examiner's attention is directed to the following co-owned, co-pending U.S. patent applications: USSNs 10/413,357; 10/336,979; 10/712,560; and 10/885,211.

Information Disclosure Statement and specification

Applicants thank the Examiner for reviewing and initialing the IDS submitted March 31, 2004. Another IDS is under preparation and will be submitted shortly. The specification is amended to correct an obvious typographical error at page 4, line 3. Entry of the amendment is respectfully requested.

Objections

The specification has been amended to capitalize trademarks as requested by the Examiner. Withdrawal of the objection is respectfully requested. With regard to the objection based on the presence of embedded hyperlinks in the specification, the specification has been reviewed and no embedded hyperlinks were found. Two citations to world wide web sites were noticed (at the locations noted by the examiner), but these are believed not to be objectionable

since they are not machine executable and are not hyperlinked. Clarification is respectfully requested from the Examiner regarding this objection.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-7, 12-15 and 17-21

Claims 1, 5-7, 12-15 and 17-21 are rejected under 35 U.S.C. § 112 first paragraph, as allegedly lacking enablement. Applicants respectfully traverse this rejection.

As a preliminary note, Applicants notes that claim 1 is directed (in part) towards an isolated nucleic acid molecule which comprises a polynucleotide having at least about 80% sequence identity to (a) a DNA molecule encoding an FGF-19 polypeptide comprising amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2) . . . ; claim 5 is directed (in part) towards an isolated nucleic acid molecule comprising a polynucleotide having at least about 80% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219) . . . ; and claim 7 is directed (in part) towards an isolated nucleic acid molecule comprising a polynucleotide having at least about 80% sequence identity to (a) the full-length polypeptide coding sequence of the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219). . . (emphasis added). Thus, it is evident that claims 1 and 5-7 are not merely directed towards "isolated nucleic acid molecules having at least 80%, sequence identity with a DNA encoding a fragment 23-216 of FGF-19 polypeptide of SEQ ID NO:2 or to a DNA comprising a fragment 550-111 of SEQ ID NO: 1" as stated in the Office Action. See, e.g., Office Action, page 3.

Turning to the rejection, the Examiner has not made a prima facie case. The law is clear that a specification which teaches how to make and use the invention in terms which correspond in scope to the claims must be taken as satisfying the enablement requirement unless there is reason to doubt the objective truth of the teachings of the specification. *In re Marzocchi*, 169 USPQ 367,369 (CCPA 1971). It is incumbent upon the Examiner to explain why one skilled in the art would doubt the truth of statements made in the specification, and provide back up assertions with acceptable and specific evidence. Id. at 370. Absent evidence to the contrary, the specification must be assumed to be enabling.

The Examiner has failed to provide acceptable and specific evidence that the specification lacks enablement. Instead, the Examiner merely opines that the specification allegedly insufficient. However, the Examiner provides no reasoning or evidence in support of this proposition. Moreover, with respect to the Examiner's assertion that "[w]hile the skill level

in the art is high, the level of predictability is low" (Office Action, page 4), Applicants respectfully point out that unpredictability and level of skill in the art are only two of several factors which must be weighed in an enablement analysis. MPEP § 2164.01(a) lists the factors to be considered, as set forth in In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). These factors include: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The MPEP states that "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others." Here, the Examiner considered only two of eight factors and ignored the other six. The factors must all be considered in an enablement analysis; no one factor is dispositive. In the Office Action, the Examiner mentions (but does not really discuss) predictability (factor E) and level of skill in the art (factor D), and does not analyze the enablement of Applicants' invention in terms of the other factors, as required by the court's decision in In re Wands and the MPEP. A rejection based on one or two of these factors alone, while ignoring the other factors, is improper.

Accordingly, Applicants submit that a prima facie case has not been made, and withdrawal of the rejection is respectfully requested.

Regarding claim 6, Applicants additionally note that claim 6 is directed towards the isolated nucleic acid molecule of Claim 5 comprising a polynucleotide encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219. Applicants submit that this claim is fully enabled and that the grounds for rejection do not apply to this claim. Withdrawal of this rejection is respectfully requested.

Applicants further submit that the specification fully enables the claims for at least the following reasons:

(1) The specification teaches amino acid and nucleic acid sequences of FGF-19;

(2) The specification teaches that standard techniques in the art may be used to make the nucleic acids of the invention, and the specification provides further guidance on how to make and use the invention in terms which correspond to the scope of the claims. For example, nucleic acid preparation is described at, e.g., pages 63-70 and Example 1, preparation of variant nucleic acids and polypeptides is described at, e.g., page 56, line 29 to page 60, line 10, determination of percent identity is disclosed at , e.g., page 22, line 25 to page 25, line 20 and Table 1; hybridization methods are described at, e.g., page 27, line 8 to page 29, line 12 and Example 2,

and methods for determining FGF-19 activity are described at, e.g., page 14, line 7 to page 15, line 27 and Examples 11-14.

(3) Making and using the nucleic acids of the invention is ascertainable through the guidance provided in the specification and (at most) routine experimentation. "Enablement is not precluded by the necessity for some experimentation such as routine screening." In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). In fact, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Id. As noted above, the specification teaches that standard techniques in the art may be used to make the nucleic acids of the invention and test the polypeptides encoded by the nucleic acids for FGF-19 activity, and the specification provides further guidance on how to make and use the invention in terms which correspond to the scope of the claims.

Review of the above-listed reasons indicates that neither undue experimentation nor a "substantial inventive contribution" (as stated by the examiner) are required to practice the claimed invention. Applicants have extensively taught how to make and use the invention in terms which correspond to the scope of the claims, methods for making and using the claimed invention are routine and known to the skilled artisan, and an ample number of working examples are provided. Accordingly, it is evident that claims 1, 5-7, 12-15 and 17-21 are fully enabled.

However, to expedite prosecution, claim 12 is canceled and claims 1, 5, and 7 have been amended, and now recite that the "polypeptide reduces total body mass in an individual, reduces fat in an individual, reduces level of triglycerides and free fatty acids in an individual, increases metabolic rate of an individual, induces leptin release from an adipocyte cell, or decreases glucose uptake in an adipocyte cell". Support for the amendment is found at least at page 14, line 7 to page 15, line 27 and Examples 11-14. Withdrawal of this rejection is respectfully requested.

Claims 1, 5-7, 12-15 and 17-21

Claims 1, 5-7, 12-15, and 17-21 are rejected under 35 U.S.C. § 112 first paragraph, as allegedly lacking written description. Applicants respectfully traverse this rejection.

The Examiner has not made a prima facie case. A description as filed is strongly presumed to be adequate. See MPEP §2163.I. The written description requirement requires that an applicant's specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); see also MPEP §2163.I.A. Compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must clearly allow a person of ordinary skill in the art to

recognize that he or she invented what is claimed. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The Examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. *See In re Wertheim*, 191 USPQ 90, 97 (CCPA 1976); see also MPEP § 2163.02.III.A.

A prima facie case as not been made because evidence has not been presented demonstrating that a person of skill in the art would not recognize in the disclosure a description of the invention defined by the claims. Instead, the Examiner merely states that the "claims do not require that the claimed polynucleotides possess any particular conserved structure, or other disclosed distinguishing feature" and that "the specification fails to describe the entire genus of nucleic acid molecules, which are encompassed by these claims". Office Action, page 6. But the Examiner does not provide evidence and reasoning in support of those statements.

By contrast, the sequence of SEQ ID NOS: 1 and 2, coupled with the recitation of percent identity (e.g., 80% identity) readily suffices to sufficiently distinguish the claimed subject matter from other materials and describe the claimed subject matter. First, Applicant submits that the amino acid sequence of SEQ ID NO:2 and/or the nucleic acid sequence of SEQ ID NO:1 are a common feature to the claimed genus. Thus, it is evident that Applicants have disclosed much more that "a partial structure in the form of a recitation of percent identity", as stated by the Examiner. Moreover, the identification of a particular portion of the sequence that must be conserved is not required under the law, contrary to the Examiner's statement in the Office Action. Second, the specification teaches (and methods are well-known in the art) how to generate nucleic acids encoding variant proteins, how to calculate percent identity of nucleic acid and amino acid sequences, and provides information relating to hybridization of nucleic acids. *See, e.g.,* specification at pages 63-70, page 56, line 29 to page 60, line 10; page 22, line 25 to page 25, line 20; Table 1; page 27, line 8 to page 29, line 12; Example 2. Indeed, it is routine for one of skill in the art to compare nucleic acid sequences and determine the percent identity of the compared sequences. The Examiner did not consider this factor in the rejection. Accordingly, withdrawal of this rejection is respectfully requested.

Regarding claim 6, Applicants further note that claim 6 is directed towards the isolated nucleic acid molecule of Claim 5 comprising a polynucleotide encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219). Applicants submit that this claim is fully described and that the grounds for rejection do not apply to this claim. Withdrawal of this rejection is respectfully requested.

However, to expedite prosecution, claim 12 is canceled and claims 1, 5, and 7 have been amended, and now recite that the "polypeptide reduces total body mass in an individual, reduces fat in an individual, reduces level of triglycerides and free fatty acids in an individual, increases metabolic rate of an individual, induces leptin release from an adipocyte cell, or decreases glucose uptake in an adipocyte cell". Withdrawal of this rejection is respectfully requested.

Claim 21

Claim 21 is also rejected under 35 U.S.C. § 112 first paragraph, as allegedly lacking enablement. Applicants respectfully traverse this rejection.

The Examiner has not made a prima facie case. The Examiner has failed to provide acceptable and specific evidence that the specification lacks enablement. Instead, the Examiner merely notes, for example, that the specification allegedly "the instant specification fails to provide any teachings on how to produce a protein, which is encoded by a nucleic acid molecule that hybridizes to the nucleic acid molecule encoding that same protein", and that "[t]he prior art does not describe any protocol on how to produce the product, as claimed". Office Action at page 9. The Examiner also states that the specification is allegedly insufficient. However, the Examiner provides no reasoning or evidence in support of those statements.

Moreover, the MPEP states that "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the [Wands] factors while ignoring one or more of the others." Here, the Examiner mentions the alleged teaching of the prior art, but does not analyze the enablement of Applicants' invention in terms of the other factors, as required by the court's decision in *In re Wands* and the MPEP. A rejection based on one of these factors alone, while ignoring the other factors, is improper.

For the above-stated reasons, Applicants respectfully request withdrawal of this rejection.

Applicants further submit that the specification fully enables the claims for at least the reasons described in the section regarding the enablement rejection of claims 1, 5-7, 12-15, and 17-21, above. Applicants further note that methods for producing protein, suitable vectors and cells and cell culture methods are well known in the art and described in the specification at, e.g., page 71, lines 1-17; page 64, line 17 to page 69, line 8; and Examples 3, 4, 5 and 6. However, claim 14 (to vectors) has been amended and now depends from claims 1 and 4. As the host cell of Claim 17 (recited in claim 21) comprises the vector of claim 14, Applicants believe that the grounds for this rejection have been obviated. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-8, 10-15 and 17-21 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants respectfully traverse.

As a preliminary matter, Applicants note that the test for definiteness under 35 U.S.C. § 112, second paragraph is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). MPEP § 2173.02 states that the Examiner must provide an analysis as to why the scope of the above-quoted limitations are allegedly indefinite.

Claims 1, 4, 9, 10, and 12

Claims 1, 4, 9, 10 and 12 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting the term "about." Applicants respectfully traverse this rejection.

The use of the term "about" does not render claims using this term indefinite. It is well established that the use of a relative term does not render a claim indefinite under 35 USC § 112, second paragraph. See Seattle Box Co. v. Industrial Crating & Packaging, Inc., 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984) (stating that the fact that the claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite); see also U.S. Patent & Trademark Office, Manual of Patent Examining Procedure § 2173.05(b). Claims are definite where "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits. As a matter of law, no court can demand more." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94, 95 (Fed. Cir. 1986).

Moreover, the term "about" is accepted and widely used in patent practice and is clearly acceptable under the law. The word "about" does not have a universal meaning in patent claims; rather, its meaning depends on the technological facts of the particular case. Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1217-18 (Fed. Cir. 1995); see also U.S. Patent & Trademark Office, Manual of Patent Examining Procedure § 2173.05(b). "About" is neither broad nor arbitrary, but rather serves as a flexible term with a meaning similar to "approximately." Conopco, Inc. v. May Dep't Stores Co., 46 F.3d 1556, 1561 (Fed. Cir. 1994); see also Ex parte Eastwood, 163 USPQ 316 (Brd. App. 1968). In Hybritech, supra, the limitation "at least about 10^8 liters/mole" was found to be definite in view of the specification and the inexact nature of the subject matter. Id. Similarly, in W.L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d 1540, 1557 (Fed. Cir. 1983), the phrase "exceeding about" was found to be definite, and in Modine Mfg. Co. v. Int'l Trade Comm'n, 75 F.3d 1545, 37 USPQ2d 1609 (Fed. Cir. 1996), the phrase "about 0.015-0.040" was found to be definite. See Modine Mfg., 721 F.2d at 1545 (stating that

"mathematical precision should not be imposed for its own sake; the patentee has the right to claim the invention in terms that would be understood by persons of skill in the art").

As a further example, Applicants direct the Examiner's attention to issued U.S. Patent Nos. 6,242,570; 6,242,214; 6, 231,864; 6,235,716; 6,235,714; 6,228,825; 6,228,825; 6, 228, 983; 6,225,442; 6,217,864; and 6,214,539, in which the word "about" is used in the claims to describe a length of a claimed polypeptide or a range of amino acids within a peptide.

Thus, it is evident that, under the law and the MPEP, the term "about" is not "inherently vague and indefinite", as stated by the Examiner in the Office Action, nor is use of the term "about" only appropriate when employed to limit a value which is composed of indefinitely divisional units, as stated by the Examiner in the Office Action. Applicants note that the Examiner cites no authority for these propositions.

Accordingly, Applicants submit that the use of the word "about" in the present application is acceptable under the law, and withdrawal of this rejection is respectfully requested.

Claim 2

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting "the sequence of nucleotide positions". Applicants traverse this rejection. Applicants submit that this rejection is improper because the Examiner has not provided an analysis as to why the scope of the above-quoted limitations are allegedly indefinite. Applicants further submit that this claim is clear, and that one of ordinary skill well understands the meaning of the above-quoted phrase. However, to clarify the claim, claim 2 has been amended and now recites "nucleotides" (rather than "the sequence of nucleotide positions"). Withdrawal of this rejection is respectfully requested.

Claims 5 and 7

Claims 5 and 7 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting "DNA which comprises at least about 80% sequence identity to [(a)] a DNA". Applicants respectfully traverse this rejection and submit that the claims are clear. However, to clarify the claim and improve consistency of claim language (compare, e.g., claim 1), claims 5 and 7 have been amended and now recite "DNA having at least 80% sequence identity" as suggested by the Examiner. Withdrawal of this rejection is respectfully requested.

Claims 11 and 12

Claims 11 and 12 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting "under stringent conditions". The Examiner states that a precise set of hybridization conditions are not provided in the claim or specification. Applicants traverse this rejection. Applicants note that "stringent hybridization" is defined in the specification at page 27,

line 20 through page 28, line 2, and that exemplary hybridization conditions are provided in the definition. See also Example 2. Accordingly, Applicants submit that the scope of the term is clear, and withdrawal of this rejection is respectfully requested. However, to expedite prosecution, claim 12 is cancelled and claim 11 as amended now recites that stringent hybridization conditions comprise 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C. Support for the amendment is found at least at page 27, line 26 to page 28, line 2 of the specification. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(b)

Claim 9 is rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Baird, et al. (1990, Handbook of Exp. Pharmacology, Chapter 7, 95 (1), pp. 369-419, reference 10 of IDS submitted on April 5, 2004). Applicants respectfully traverse this rejection.

The Examiner has provided no evidence or reasoning in support of her conclusion that "any nucleic acid, encoding a fibroblast growth factor would anticipate the nucleic acid of claim 9". Accordingly, a prima face case of anticipation has not been made and withdrawal of the rejection is respectfully requested. However, claim 9 has been amended and now recites "stringent hybridization" and provides conditions for stringent hybridization. Accordingly, Applicants believe that the grounds for this rejection have been obviated. Withdrawal of this rejection is respectfully requested.

SUMMARY

Applicants believe that this application is now in condition for allowance and respectfully requests that the outstanding rejections be withdrawn and this case passed to issue. No new matter has been introduced, and entry of these amendments is respectfully requested. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is strongly encouraged to call the undersigned at the number indicated below.

This response/amendment is submitted with a transmittal letter and petition for a 3-month extension of time and fees. In the unlikely event that this document is separated from the transmittal letter or if fees are required, applicants petition the Commissioner to authorize

charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,
GENENTECH, INC.

Date: 1/18/05

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